BAB 5
KESIMPULAN DAN SARAN

5.1. Kesimpulan

Berdasarkan hasil analisis data dan interpretasi penelitian dapat disimpukan bahwa metode KCKT dengan fase diam kolom fase balik C-18 dengan kecepatan aliran 1 ml/menit, ukuran pori 10 μm (LiChrospher® 100, Germany) dan fase gerak metanol : air (65 : 35 v/v) dapat digunakan untuk melakukan analisis kuantitatif yang akurat dan selektif untuk mengidentifikasi dan menetapkan kadar tadalafil. Dari hasil analisis sampel permen karet cinta yang dibeli secara *online* tidak ditemukan kandungan tadalafil di dalamnya.

5.2. Saran

Berdasarkan hasil yang sudah diperoleh, disarankan untuk melakukan penelitian lebih lanjut untuk mengidentifikasi zat apa yang sebenarnya terkandung dalam permen karet cinta. Bisa dimulai dengan menetapkan beberapa senyawa yang kemungkinan besar bisa memberikan efek peningkatan libido pada wanita yang memiliki sifat yang hampir sama atau berasal dari golongan yang sama dengan tadalafil atau dengan meneliti beberapa sediaan lainnya yang beredar di pasaran yang memiliki efek peningkatan libido wanita.

DAFTAR PUSTAKA

Accessr Medications Online, **Cialis For Woman**, http://www.accessrx.com, 28 Agustus 2013.

Badan Intelijen Negara RI, 2013, **Bahaya di Balik Permen Cinta**, http://www.bin.go.id, 25 Februari 2013.

Balai POM, 2012, **Pedoman Pemberian Sertifikat Produksi Pangan Industri Rumah Tangga**, BPOM, Jakarta.

Belitz, H . D. and W. Grouch, 1987, **Food Chemistry**, 2nd ed, Heilderberg, Spinger-Verlag, Berlin, 232.

Bliesner, D. M., 2006, **Validating Chromatographic Methods A Practical Guide**, John Wiley and son, Inc., New Jersey, 8.

Bolton, S., and C. Bon, 2004, **Pharmaceutical Statistics Practical and Clinical Application**, Marcel Dekker Inc**,** New York.

BPOM RI, 2013, **Pengawasan Produk Permen Peningkat Gairah atau Libido**, http://www.pom.go.id, 31 Januari 2013.

Carlson *et al.*, 2002, **Gum Chewing May Help,** http:// findarticles.com, 27 Agustus 2013.

Clark, J., 2007, **High Performance Liquid Chromatography – HPLC**, http://www.chemguide.co.uk, 17 September 2013.

Damayanti, S., 2005. **Manfaat Permen Karet bagi Kesehatan**. http://www.pikiran-rakyat.co.id, 03 April 2013.

Deinstrop, E. H., 2000. **Applied Thin Layer Chromatography**. Willey-VCH, New York, 1, 67, 150.

Department of Chemistry University Adelaide, **Photodiode Array Detectors (PDA),** http://www.chemistry.adelaide.edu, 30 Agustus 2013.

Duangteraprecha,S.,Ph.D., 2000, Asean Guidlines for Validation of Analytical Procedures, http://www.docstoc.com, 20 September 2013.

Epshtein, N. A., 2004, Validation of HPLC Techniques for Pharmaceutical Analysis, **Pharmaceutical Chemistry Journal**, vol. 38(4), 228.

Ermer, J., 2005, Analitical Validation within the Pharmaceutical Environment, in: **Method Validation in Pharmaceutical Analysis**, Wiley-VCH Verlag GmbH & Co. KgaA, Weinheim, 3-5, 16.

Green, J. M., 1996. Practical Guide to Analytical Method Validation, **Analytical Chemistry**.Vol.II, 305.

Harmita, 2004, Petunjuk Pelaksanaan Validasi Metode dan Cara Perhitungannya, dalam: **Majalah Ilmu Kefarmasian**, Vol., I, nomor 3, 117-132.

Heftmann, E., 2004, Chromatography 6th Edition Part A : Fundamentals and Techniques, Elevier, Netherlands, 96-125.

Keller, Heckman, Belgum., 2007, **International chewing gum association**, http://www.gumassociation.org, 29 Agustus 2013.

Lawrence, 2012, The United State Pharmacopeia, 35th ed., Electronic Version, United States, Vol.1, 878-881.

Lindsay, S., and D. Kealey, 1991, High Performance Liquid Chromatography, John Wiley and Sons, Ltd., Singapore.

Lund, W., 1994, **The Pharmaceutical Codex 12th**, The Pharmaceutical Press, London.

Madan, N., and A. Rathnan, 2011, Chewing Gums for Optimal Health, dalam: **Chronicles of Young Scienstists**, Vol 2 (1), 8.

Madhavy, A., G. S. Reddy., M. V. Suryanarayana and A. Naidu, 2008, Chiral separation of (r,r)-tadalafil and its enantiomer in bulk drug samples and pharmaceutical dosage forms by chiral RP-LC, dalam: **Chromatographia**, v.67, n.7-8, p.633-638.

MedlinePlus, 2012, Tadalafil, http://www.nlm.gov, 29 Agustus 2013.

Mulja, M., dan A. Syahrani, 1991, KCKT (Kromatografi Cair Kinerja Tinggi) Teori Dasar, Instrumentasi dan Aplikasi, Mecphiso Grafika, Surabaya.

Pills for us, 2013, **Cialis – Effectiveness of Cialis for Woman**, http://pills4us.com, 28 Agustus 2013.

Redaksi, 2013, **Laporan Khas Redaksi: Kandungan Permen Cinta Sama Dengan Viagra**, Trans 7, Jakarta, 14 Februari 2013.

Rohman, A., and I.G. Gandjar, 2007, **Kimia Farmasi Analisis, cetakan pertama**, Pustaka Pelajar, Yogyakarta.

Roth, J., and G. Blaschke, 1998, **Analisis Farmasi**, terjemahan S. Kisman dan S. Ibrahim, Penerbit UGM, Yogyakarta, 402-424.

Samala, A., S. Pawar., S. Manala., S. Chada and M. Nageshwar, 2013, RP-HPLC Method Development and Validation of Tadalafil in Tablet Dosage Form, Journal of Chemical and Pharmaceutical Research, www.jocpr.com. 28 Agustus 2013.

Skoog, D.A., and D. M. West, 1980, **Principle of Instrumental Analysis**, Thomson Higher Education, London, 816-832.

Sutar, A. S., C. S. Magdum, S. S. Patil, N. S. Naikawadi, 2008, RP-HPLC Estimation of Tadalafil in Tablet Dosage Form, Sadguru Publication, Undaipur India.

Swadesh, J. K., 2000, HPLC Pratical and Industrial Applications 2nd Edition, CRC Press, Boca Raton Florida, 2-18;141-166.

Sweetman, S. C., 2009, **Martindale: The Complete Drug reference**, 36th ed, Pharmaceutical Press, London, 2196-2197.

Thomas, G., 2000, Medicinal Chemistry, Jhon Wiley & sons, New York, 456-457.

Watson, D. G., 2009, **Analisis Farmasi**, penerjemah : W. R. Syarif, Penerbit Buku Kedokteran EGC, Jakarta, 380.

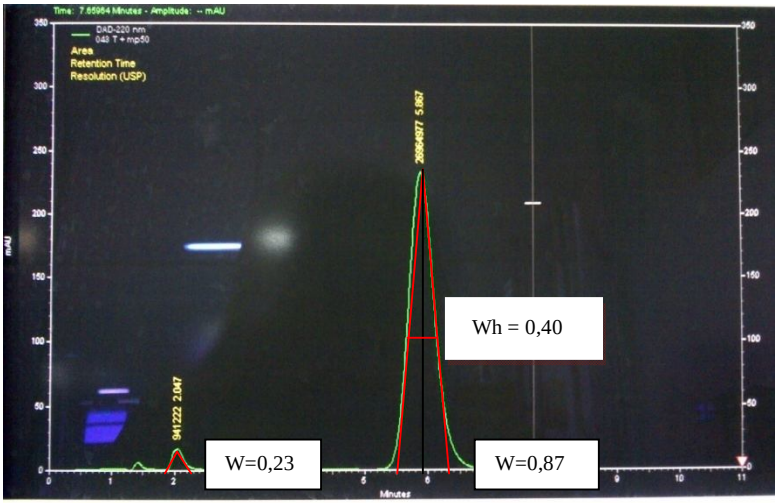
Yang, Y. J., D. M. Song, W. M. Jiang, B. R. Xiang, 2009, Rapid Resolution RP-HPLC-DAD Method for Simultaneous Determination of Sidenafil, Verdenafil and Tadalafil in Pharmaceutical Preparations and Counterfeit Drugs, dalam: Analytical Letters, Vol. 43 (3).

Zaimu, A, 2013, Permen Karet Cinta Bangkitkan Hasrat Seksual dalam 20 Menit, http://www.tribunnews.com, 6 Februari 2013.

Zhu, X., S. Xiao., B. Chen., F. Zhang., S. Yao., Z. Wan., D. Yang and H. Han, 2005, Simultaneous Determination of Sildenafil, Verdenafil and Tadalafil as Forbidden Components in Natural Dietary Supplements for Male Sexual Potency by High Performance Liquid Chromatography Electrospray Ionization Mass Spectrometry, Journal of Chromatography A, www.elsevier.com/locate/chroma, 28 Agustus 2013.

Lampiran 1.

Contoh Perhitungan Rs, k' dan N



Peak tadalafil dengan matriks perman karet pertama menggunakan fase gerak (4) metanol : air (65 : 35 v/v)

Rt tadalafil : 5,867

Rt matriks : 2,047

W tadalafil : 0,87

W matriks : 0,23

Rt_0 :1,487

Wh : 0,40

$$Rs = \frac{2(\Delta Z)}{WA+WB}$$

$$Rs = \frac{2(5,867 - 2,047)}{0,87 + 0,23}$$

Rs = 5,95

$$k' = \frac{(Rt_{\text{tadalafil}} - Rt_0)}{Rt_0}$$

$$k' = \frac{(5,867 - 1,487)}{1,487}$$

$$k' = 2,95$$

$$N = 5,545\left[\frac{Rt}{Wh}\right]^2$$

$$N = 5,545\left[\frac{5,867}{0,40}\right]^2$$

$$N = 1192,93$$

Lampiran 2.

Perhitungan Harga F

Hari	Konsentrasi (ppm) (X)	Luas Area Rata-Rata (Y)	X^2	Y^2	XY
1	12,42	6.707.656,50	154,26	44.992.655.721.992,20	83.309.093,73
	34,78	20.005.316,50	1.209,65	400.212.688.265.172,00	695.784.907,87
	54,65	32.295.735,50	2.986,62	1.043.014.531.485.960,00	1.764.961.945,08
	79,49	45.696.506,50	6.318,66	2.088.170.706.304.540,00	3.632.415.301,69
	99,37	56.882.309,50	9.874,40	3.235.597.134.053.790,00	5.652.395.095,02
		Σ=	$20,5 \times 10^2$	$68,1 \times 10^{14}$	$11,8 \times 10^9$
2	12,43	6.668.689,00	154,50	44.471.412.978.721,00	82.891.804,27
	34,82	18.974.135,00	1.212,43	360.017.798.998.225,00	660.679.380,70
	54,71	29.403.719,00	2.993,18	864.578.691.030.961,00	1.608.677.466,49
	79,58	44.471.839,50	6.332,98	1.977.744.508.513.760,00	3.539.068.987,41
	99,48	55.808.190,50	9.896,27	3.114.554.126.884.290,00	5.551.798.790,94
		Σ=	$20,6 \times 10^2$	$63,6 \times 10^{14}$	$11,4 \times 10^9$
3	12,54	7.569.320,00	157,25	57.294.605.262.400,00	94.919.272,80
	35,11	18.747.306,50	1.232,71	351.461.501.004.942,00	658.217.931,22
	55,17	32.888.095,00	3.043,73	1.081.626.792.729.020,00	1.814.436.201,15
	80,24	48.362.743,50	6.438,46	2.338.954.958.846.790,00	3.880.626.538,44
	100,30	60.996.599,00	10.060,09	3.720.585.089.566.800,00	6.117.958.879,70
		Σ=	$20,9 \times 10^2$	$75,5 \times 10^{14}$	$12,6 \times 10^9$

Hari	Σ x²	Σ xy	Σ y²	Residual SS	N	Residual DF (n-2)
I	20,5 x 102	11,8 x 109	68,1 x 1014	4,39 x 1013	5	3
II	20,6 x102	11,4 x 109	63,6 x 1014	4,61 x 1013	5	3
III	20,9 x 102	12,6 x 109	75,5 x 1014	4,59 x 1013	5	3
Σ=	62,0 x 102	35,8 x 109	20,7 x 1015	1,36 x 1014		9

SS1 $= \Sigma y^2 1 - \frac{\Sigma\, xy^2}{\Sigma x^2} = 68{,}1 \times 10^{14} - \frac{1{,}39x10^{20}}{20{,}5 \times 10^{2}} = -\,6{,}11 \times 10^{16}$

SS2 $= \Sigma y^2 2 - \frac{\Sigma\, xy^2}{\Sigma x^2} = 63{,}6 \times 10^{14} - \frac{1{,}30x10^{20}}{20{,}6 \times 10^{2}} = -\,5{,}67 \times 10^{16}$

SS3 $= \Sigma y^2 3 - \frac{\Sigma\, xy^2}{\Sigma x^2} = 75{,}5 \times 10^{14} - \frac{1{,}59x10^{20}}{20{,}9 \times 10^{2}} = -\,6{,}84 \times 10^{16}$

SSt = SS1 + SS2 + SS3

$= (-6{,}11 \times 10^{16}) + (-5{,}67 \times 10^{16}) + (-6{,}84 \times 10^{16})$

$= -18{,}62 \times 10^{16}$

SSc $= \Sigma\,(\Sigma y^2) - \frac{\Sigma\,(\Sigma xy)^2}{\Sigma(\Sigma x^2)} = 20{,}7 \times 10^{15} - \frac{1{,}28\,x\,10^{21}}{62.065{,}19} = -\,18{,}60 \times 10^{16}$

F $= \frac{\frac{SSc-SSt}{DF-1}}{\frac{SSt}{DFt}} = \frac{\frac{18{,}60 \times 10^{16} - 18{,}62\,x\,10^{16}}{3-1}}{\frac{18{,}62 \times 10^{16}}{9}} = -\,0{,}0048$

F hitung = 0,0048

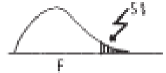
$F\ tabel_{0{,}05(2:9)} = 4{,}26$

F hitung < F tabel = 0,0048 < 4,26 = tidak ada perbedaan yang bermakna (H_0 diterima)

Lampiran 3.

F tabel

Table IV.6A Upper 5% Values of the *F* Distribution[a]



Degrees of freedom in denominator	Degrees of freedom in numerator												
	1	2	3	4	5	6	7	8	9	10	20	40	∞
1	161	200	216	225	230	234	237	239	241	242	248	251	254
2	18.5	19.0	19.2	19.2	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.5	19.5
3	10.1	9.55	9.28	9.12	9.01	8.94	8.89	8.85	8.81	8.79	8.66	8.59	8.53
4	7.71	6.94	6.59	6.39	6.26	6.16	6.09	6.04	6.00	5.96	5.80	5.72	5.63
5	6.61	5.79	5.41	5.19	5.05	4.95	4.88	4.82	4.77	4.74	4.56	4.46	4.37
6	5.99	5.14	4.76	4.53	4.39	4.28	4.21	4.15	4.10	4.06	3.87	3.77	3.67
7	5.59	4.74	4.35	4.12	3.97	3.87	3.79	3.73	3.68	3.64	3.44	3.34	3.23
8	5.32	4.46	4.07	3.84	3.69	3.58	3.50	3.44	3.39	3.35	3.15	3.04	2.93
9	5.12	4.26	3.86	3.63	3.48	3.37	3.29	3.23	3.18	3.14	2.94	2.83	2.71
10	4.96	4.10	3.71	3.48	3.33	3.22	3.14	3.07	3.02	2.98	2.77	2.66	2.54
11	4.84	3.98	3.59	3.36	3.20	3.09	3.01	2.95	2.90	2.85	2.65	2.53	2.40
12	4.75	3.89	3.49	3.26	3.11	3.00	2.91	2.85	2.80	2.75	2.54	2.43	2.30
13	4.67	3.81	3.41	3.18	3.03	2.92	2.83	2.77	2.71	2.67	2.46	2.34	2.21
14	4.60	3.74	3.34	3.11	2.96	2.85	2.76	2.70	2.65	2.60	2.39	2.27	2.13
15	4.54	3.68	3.29	3.06	2.90	2.79	2.71	2.64	2.59	2.54	2.33	2.20	2.07
16	4.49	3.63	3.24	3.01	2.85	2.74	2.66	2.59	2.54	2.49	2.28	2.15	2.01
17	4.45	3.59	3.20	2.96	2.81	2.70	2.61	2.55	2.49	2.45	2.23	2.10	1.96
18	4.41	3.55	3.16	2.93	2.77	2.66	2.58	2.51	2.46	2.41	2.19	2.06	1.92
19	4.38	3.52	3.13	2.90	2.74	2.63	2.54	2.48	2.42	2.38	2.16	2.03	1.88
20	4.35	3.49	3.10	2.87	2.71	2.62	2.51	2.45	2.39	2.35	2.12	1.99	1.84
25	4.24	3.39	2.99	2.76	2.60	2.49	2.40	2.34	2.28	2.24	2.01	1.87	1.71
30	4.17	3.32	2.92	2.69	2.53	2.42	2.33	2.27	2.21	2.16	1.93	1.79	1.62
40	4.08	3.23	2.84	2.61	2.45	2.34	2.25	2.18	2.12	2.08	1.84	1.69	1.51
120	3.92	3.07	2.68	2.45	2.29	2.18	2.09	2.02	1.96	1.91	1.66	1.50	1.25
∞	3.84	3.00	2.60	2.37	2.21	2.10	2.01	1.94	1.88	1.83	1.57	1.39	1.00

[a] For degrees of freedom not included in the table, interpolate using the reciprocal of degrees of freedom. For example, $F_{1,60}$ is between 4.08 and 3.92. 1/40 = 0.025; 1/120 = 0.0083; 1/60 = 0.0167, which is halfway between 1/120 and 1/40. Therefore, $F_{1,60}$ = 4.00.

Lampiran 4.

Perhitungan harga t

- 25 ppm (50%) :

$$t = \frac{|\bar{x}\text{-}100|}{\sqrt{\frac{SD^2}{N}}}$$

$$t = \frac{|102{,}16\text{-}100|}{\sqrt{\frac{3{,}16^2}{3}}}$$

$t = 0{,}65$

- 50 ppm (100%) :

$$t = \frac{|\bar{x}\text{-}100|}{\sqrt{\frac{SD^2}{N}}}$$

$$t = \frac{|99{,}64\text{-}100|}{\sqrt{\frac{2{,}83^2}{3}}}$$

$t = 0{,}13$

- 75 ppm (150%) :

$$t = \frac{|\bar{x}\text{-}100|}{\sqrt{\frac{SD^2}{N}}}$$

$$t = \frac{|99{,}53\text{-}100|}{\sqrt{\frac{0{,}71^2}{3}}}$$

$t = 2{,}79$

Lampiran 5.

t tabel

Table IV.4 *t* Distributions

Two-sided:	40%	20%	10%	5%	1%
One-sided:	20%	10%	5%	2.5%	0.5%
d.f.:	$t_{0.80}$	$t_{0.90}$	$t_{0.95}$	$t_{0.975}$	$t_{0.995}$
1	1.38	3.08	6.31	12.71	63.66
2	1.06	1.89	2.92	4.30	9.92
3	0.98	1.64	2.35	3.18	5.84
4	0.94	1.53	2.13	2.78	4.60
5	0.92	1.48	2.02	2.57	4.03
6	0.91	1.44	1.94	2.45	3.71
7	0.90	1.42	1.89	2.36	3.50
8	0.89	1.40	1.86	2.31	3.36
9	0.88	1.38	1.83	2.26	3.25
10	0.88	1.37	1.81	2.23	3.17
11	0.88	1.36	1.80	2.20	3.11
12	0.87	1.36	1.78	2.18	3.05
13	0.87	1.35	1.77	2.16	3.01
14	0.87	1.35	1.76	2.14	2.98
15	0.87	1.34	1.75	2.13	2.95
16	0.86	1.34	1.75	2.12	2.92
17	0.86	1.33	1.74	2.11	2.90
18	0.86	1.33	1.73	2.10	2.88
19	0.86	1.33	1.73	2.09	2.86
20	0.86	1.33	1.72	2.09	2.85
25	0.86	1.32	1.71	2.06	2.79
30	0.85	1.31	1.70	2.04	2.75
40	0.85	1.30	1.68	2.02	2.70
60	0.85	1.30	1.67	2.00	2.66
120	0.85	1.29	1.66	1.98	2.62
∞	0.84	1.282	1.645	1.96	2.576

Lampiran 6.

Perhitungan % KV

- 25 ppm (50%) :

$$\%KV = \frac{SD}{\bar{X}} x100\%$$

$$\%KV = \frac{3,16}{102,16} x100\%$$

$$\%KV = 3,09\%$$

- 50 ppm (100) :

$$\%KV = \frac{SD}{\bar{X}} x100\%$$

$$\%KV = \frac{2,83}{99,64} x100\%$$

$$\%KV = 2,84\%$$

- 75 ppm (150%) :

$$\%KV = \frac{SD}{\bar{X}} x100\%$$

$$\%KV = \frac{0,71}{99,53} x100\%$$

$$\%KV = 0,71\%$$

Lampiran 7.

R tabel

df = (N-2)	Tingkat signifikansi untuk uji satu arah				
	0.05	0.025	0.01	0.005	0.0005
	Tingkat signifikansi untuk uji dua arah				
	0.1	0.05	0.02	0.01	0.001
1	0.9877	0.9969	0.9995	0.9999	1.0000
2	0.9000	0.9500	0.9800	0.9900	0.9990
3	0.8054	0.8783	0.9343	0.9587	0.9911
4	0.7293	0.8114	0.8822	0.9172	0.9741
5	0.6694	0.7545	0.8329	0.8745	0.9509
6	0.6215	0.7067	0.7887	0.8343	0.9249
7	0.5822	0.6664	0.7498	0.7977	0.8983
8	0.5494	0.6319	0.7155	0.7646	0.8721
9	0.5214	0.6021	0.6851	0.7348	0.8470
10	0.4973	0.5760	0.6581	0.7079	0.8233
11	0.4762	0.5529	0.6339	0.6835	0.8010
12	0.4575	0.5324	0.6120	0.6614	0.7800
13	0.4409	0.5140	0.5923	0.6411	0.7604
14	0.4259	0.4973	0.5742	0.6226	0.7419
15	0.4124	0.4821	0.5577	0.6055	0.7247
16	0.4000	0.4683	0.5425	0.5897	0.7084
17	0.3887	0.4555	0.5285	0.5751	0.6932
18	0.3783	0.4438	0.5155	0.5614	0.6788
19	0.3687	0.4329	0.5034	0.5487	0.6652
20	0.3598	0.4227	0.4921	0.5368	0.6524
21	0.3515	0.4132	0.4815	0.5256	0.6402
22	0.3438	0.4044	0.4716	0.5151	0.6287
23	0.3365	0.3961	0.4622	0.5052	0.6178
24	0.3297	0.3882	0.4534	0.4958	0.6074
25	0.3233	0.3809	0.4451	0.4869	0.5974
26	0.3172	0.3739	0.4372	0.4785	0.5880
27	0.3115	0.3673	0.4297	0.4705	0.5790

Lampiran 8.

Perhitungan LOD & LOQ

$$S\frac{y}{x} = \sqrt{\frac{\sum(Y-Yi)^2}{n-2}} = \sqrt{\frac{6{,}73 \times 10^{10}}{8-2}}$$

$$S\frac{y}{x} = 105.908{,}76$$

$$LOD = \frac{3 \times s\frac{y}{x}}{slope} = \frac{3 \times 105.908{,}76}{522.069{,}52}$$

LOD = 0,61 ppm

Baku induk = 499,7 ppm (penimbangan 92,1 mg tadalafil).

$$LOD = \frac{0{,}61 \text{ ppm}}{499{,}7 \text{ ppm}} \text{ x } 92{,}1 \text{ mg}$$

LOD = 0,11 mg tadalafil / permen karet

$$LOQ = \frac{10 \times s\frac{y}{x}}{slope} = \frac{10 \times 105.908{,}76}{522.069{,}52}$$

LOQ = 2,03 ppm

Baku induk = 499,7 ppm (penimbangan 92,1 mg tadalafil).

$$LOQ = \frac{2{,}03 \text{ ppm}}{499{,}7 \text{ ppm}} \text{ x } 92{,}1 \text{ mg}$$

LOQ = 0,37 mg tadalafil / permen karet

Lampiran 9.

Daftar Penimbangan Tadalafil

Linieritas, Akurasi dan Presisi

Hari	Berat Tablet (mg)	Penimbangan (mg)	Jumlah Tadalafil (mg)	Konsentrasi (ppm)
Pertama	362,3	90,0	4,9683	496,83
Kedua	362,3	90,1	4,9738	497,38
Ketiga	361,3	90,6	5,0152	501,52

LOD & LOQ

Berat tablet tadalafil = 368,62 mg

Penimbangan = 92,1 mg

Jumlah tadalafil = 4,997 mg

Konsentrasi baku induk tadalafil = 499,7 ppm